Pain Management in the Surgical Patient

Peter Vogel, VMD, DACVS

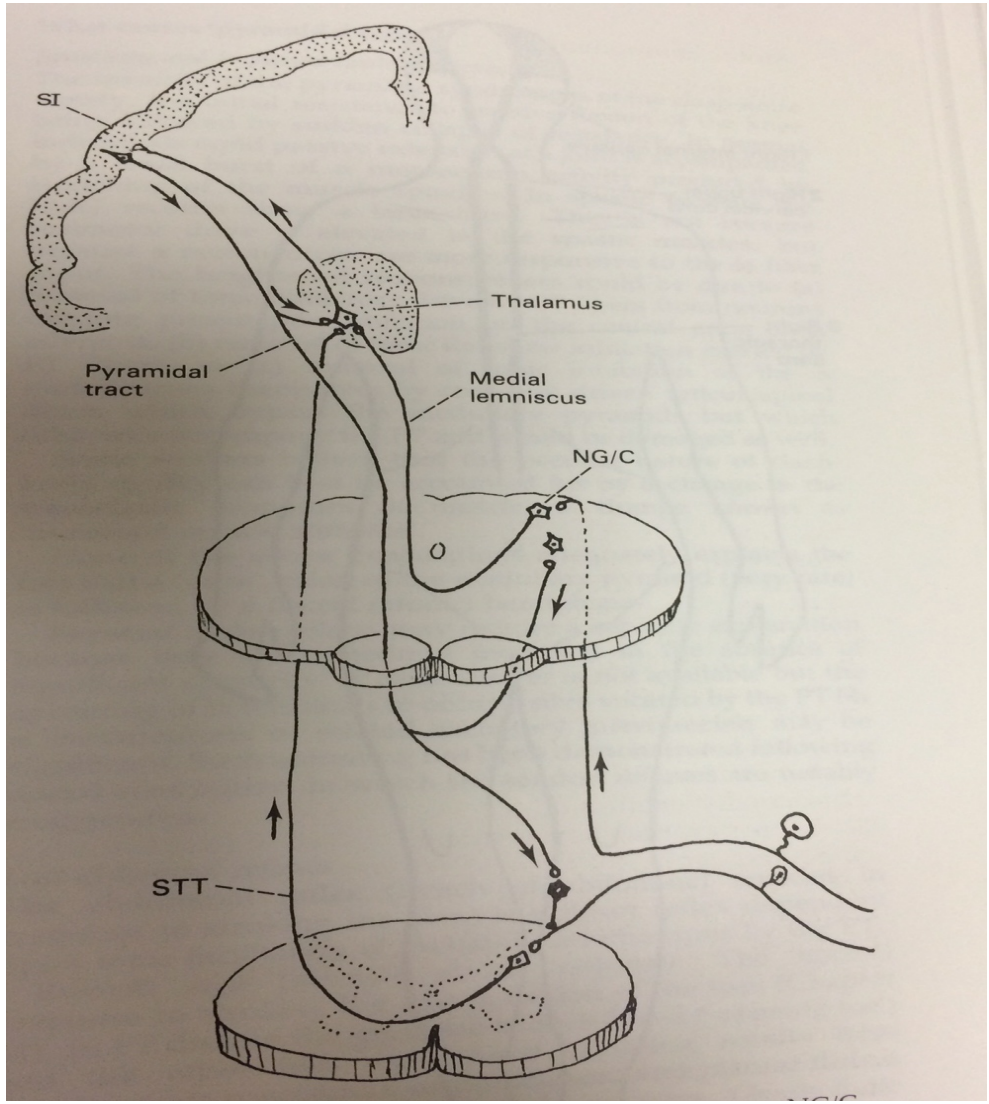
West Coast Specialty and Emergency Animal Hospital

Pain Pathways

- Specialized neurons that travel through the spinal cord
- Free nerve endings in skin, connective tissue, muscle and bone
- Cell bodies in the dorsal root ganglia

Pain Pathways

- Afferent system consisting of 3 neurons
- Cell body that bifurcates with one end in the peripheral tissue and one in the dorsal horn
- Second order neurons ascend in the contralateral spinothalamic tract
- Third order neurons in the contralateral thalamus project to the somatosensory cortex


SI
Thalamus
Pyramidal tract
Medial lemniscus
NG/C
STT

Acute Pain

- Acute pain is usually nociceptive pain
- Tissue damage leads to activation of small nerve endings and inflammatory cells
- Inflammatory mediators cause pain via nociceptive stimulation and increased excitability of nerve endings
- NOTE: Complex system, not just neurons involved**

- Pain management strategies should target as many aspects of the nociceptive response as possible
- Variety of pain receptors and mediators can be manipulated and controlled via pharmacologic intervention.

Pre-operative Medications

- All surgical patients should have pre-operative pain medication
  - General anesthesia blocks the brain from feeling pain, but does not prevent activation of the local and spinal pain pathways (ramp up)
  - It is better to prevent stimulation of the nociceptive pathways than try and treat them post-operatively.

Pre-operative Medications

- Nociceptive pathways are activated both by inflammation and direct neuron stimulation
  - Narcotics will help decrease neuronal stimulation
  - NSAIDS will help minimize inflammatory stimulation
- Unless contra-indicated, both should be given

Butorphanol

- Mixed agonist-antagonist
- More sedatory than analgesic
- Fairly rapid onset
- Analgesia lasts 1-3 hours
- Bonds more tightly than pure agonists
- Appropriate for mild-moderate pain only

Buprenorphine

- Partial Mu agonist
- SLOW ONSET (20 minutes minimum)
- Lasts 4-8 hours at common dosages
- Used for mild-moderate pain
- Well tolerated in cats
- **Buprenorphine** displaces morphine, methadone, and other full opioid agonists from receptors. It also can block the effects of other opioids.
- Extreme receptor affinity (not reversed by naloxone) but low intrinsic activity

- The main reason for use of butorphanol and buprenorphine in the past was that they were not controlled substances
- There are better narcotics for use in operative patients

Morphine

- Prototypical opioid
- Onset of action 15-30 minutes
- Hepatic metabolism and renal excretion (use with caution in patients with renal disease)
- Can be used in cats!!
  - “Morphine Mania” is due to inappropriately high doses in cats
  - Causes mydriasis rather than miosis in cats

Morphine

- Cardiovascular depression
- Dose dependent respiratory depression
- Low lipid solubility (slow onset IV), useful for epidural injection
- Can be given intra-articularly (0.1 mgs/kg diluted in saline)
- Oral forms have low bio-availability
- Histamine release

Hydromorphone/Oxymorphone

- 5-10X more potent than morphine
- Does not cause histamine release
- 15-20 minute onset of action IV, lasts 2-6 hours
- Much slower onset when given IM or SQ
- Hyperthermia in cats (not responsive to naloxone)
  - Must monitor temperature

Fentanyl

- 100X more potent than morphine
- High lipid solubility = rapid onset of action
- Rapidly redistributed = short duration of action
- Can be given IV, IM, epidurally, transmucosally, and transdermally
- Usually given as an IV bolus followed by a CRI

Methadone

- Methadone is a mu-receptor (OP3; MOR) agonist that also is a non-competitive inhibitor of NMDA (n-methyl-d-aspartate) receptors. Methadone can also reduce re-uptake of norepinephrine and serotonin, which may contribute to its analgesic effects. Due to these other actions, methadone potentially may be more efficacious than other mu- agonists (e.g., morphine) particularly for neuropathic or chronic pain. Methadone is more lipid-soluble than morphine and approximately 1-1.5X as potent. It does not cause significant histamine release when administered intravenously.

Methadone

- Usually given as an IV CRI
- Can be dosed IV, IM, and SC

NSAIDS

- Unless contra-indicated, all surgical patients should receive injectable NSAIDs pre-operatively
- Yes, you can give NSAIDs to cats
  - Meloxicam (0.05-0.1 mgs/kg IV/SQ)
  - Robenicoxib (Onsior) (2 mgs/kg IV/SQ)
- Reduces inflammation and release of inflammatory mediators

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Comparison of injectable robenacoxib versus meloxicam for peri-operative use in cats: results of a randomised clinical trial.

Kamata M[1], King JN, Seewald W, Sakakibara N, Yamashita K, Nishimura R.

Author information

Abstract

The objective of this study was to evaluate the efficacy and tolerability of robenacoxib, a selective cyclooxygenase-2 inhibitor, for the treatment of post-operative pain and inflammation in cats. The study was a prospective, multi-centre, randomised, blinded, non-inferiority design clinical study to compare robenacoxib to meloxicam. Ninety-six cats undergoing surgery at eight centres in Japan were allocated randomly to receive a single s.c. injection of robenacoxib (2 mg/kg, n=67) or meloxicam (0.3 mg/kg, n=29) shortly before induction of anaesthesia. Most cats underwent soft tissue surgery (n=87), mainly ovariectomy (n=68). Post-operative pain and inflammation were assessed at 3, 8 and 22 h after recovery from anaesthesia using numerical rating scales. For the primary efficacy endpoint (total clinician score), robenacoxib had significantly better efficacy than meloxicam, the relative efficacy ratio being 1.47 (95% confidence interval 1.19-1.78, P=0.0003). For the secondary efficacy endpoints, robenacoxib was superior to meloxicam when assessed on the basis of posture, behaviour, pain on palpation and overall pain control, while meloxicam was superior with respect to wound heat. No cat in either group required rescue analgesia therapy. In tolerability assessments, pain during injection and pain and inflammation at the injection site 22 h after recovery from anaesthesia were rated significantly less with robenacoxib compared to meloxicam. Both treatments were well tolerated on the basis of clinical observations and blood tests, with no significant differences between groups. In conclusion, single pre-operative administration of robenacoxib was well tolerated and had superior efficacy to meloxicam in reducing post-operative pain in cats.

PMID: 22227226 [PubMed - indexed for MEDLINE]

Publication Types, MeSH Terms, Substances

LinkOut - more resources

Post-operative Pain Management

- If your pre-operative protocol is effective, post-operative pain management will be much easier
- Far easier to prevent activation of nociceptive pathways than to suppress them later

Pain Assessment

- CSU pain score chart (see handout)
- Cats and dogs show pain differently
- If in doubt, assume the patient is painful
- Best indication is behavior

Pain vs Dysphoria

- Can be difficult to differentiate pain vs. dysphoria secondary to general anesthesia
- Micro-dose Dexmedetomidine test:
  - 1-2 mcg/kg IV
  - If dysphoric, patient will respond
  - If painful, minimal response seen

Opioids

- All patients should receive post-operative opioid analgesia
- Dosages and effects/actions similar to pre-operative
- Vomiting post-operatively from opioids is uncommon

Butorphanol

- Useful for mild-moderate pain
- Slow onset, short duration of action for analgesia, longer for sedation
- Often combined with dexmedetomidine or acepromazine
  - Caution in compromised patients
- Probably should not be used for any patient where significant pain is anticipated
- Pure agonist can be administered if needed

Buprenorphine

- Very slow onset of action
- Threshold effect (giving more does not increase pain relief)
- Higher doses do, however, last longer
  - 50 mcg/kg will last 24 hours
- Cannot give any other opioid if buprenorphine is not effective due to high binding affinity
- Can be used to reverse other opioid without removing all pain control

Hydromorphone/Oxymorphone

- Commonly given at 0.1 mg/kg q 4-6 hrs as needed
- Dose can be increased if necessary
- Given IV, IM, or SQ

Methadone

- Effective as CRI or as intermittent dosing (q4-6 hrs)
- Slightly more effective than morphine

Methadone

- Dogs: 0.1-0.2 mgs/kg IV followed by CRI @ 0.12 mgs/kg/hr OR 0.1-1.0 mg/kg q4-8 hrs IV. IM, SQ
- Cats: 0.1-0.2 mgs/kg IV followed by CRI @ 0.12 mgs/kg/hr OR 0.05-0.5 mg/kg q 4-6 hrs IV, IM, SQ

- Oral form poorly absorbed

Fentanyl

- Usually used as a CRI (2-8 mcg/kg/hr)
- Requires infusion pump
- Bolus can be given and CRI rate increased if pain control inadequate
- CRI should be tapered over 12-24 hours as other pain control medications are taking effect.
- Very short duration

Medications TGH

- What options do we have?
- How effective are they?

Oxycodone

- Poor bioavailability
- High potential for abuse by owner

Codeine

- Poor bioavailablity

Acetaminophen/Hydrocodone

- Acetaminophen is ineffective but well tolerated in dogs as long as the dosage is not too high
- Acetaminophen is highly toxic to cats

- 0.22-0.5 mg/kg Hydrocodone
- ***DO NOT EXCEED 15 MG/KG ACETAMINOPHEN***
  - *20 kgs or larger for tablets*

Fentanyl Patch

- 12-24 hours for onset (should be used with another agonist initially)
- Can be removed if side effects are significant
- Potential for abuse by owner
- Potential for accidental exposure to owner
- Potential for accidental ingestion by pet
- Typically lasts 72-96 hours

Fentanyl Patch

- Available from 12-100 mcg/hr, sized by weight of patient
- DO NOT CUT PATCH
- Can use more than one patch if patient over 40 kgs
- Variable absorption
  - Dependent on placement, adherence, obesity, temperature

Transdermal Fentanyl (Recuvrya)

- Super-concentrated form of fentanyl for transdermal absorption
- Rapid onset of action (2 hours or less)
- Lasts up to 5 days

Transdermal Fentanyl

- Like all “depo” drugs, it cannot be removed if side effects occur
  - Dysphoria
  - Urine retention
  - Excessive sedation
- Requires continual reversal to overcome side effects for many days
  - High dose buprenorphine daily
  - Naloxone q 4-6 hours

Tramadol

- Unlike in people and cats, dogs **do not metabolize** Tramadol to the active form (M1) to any significant degree
- Minimal narcotic effect in dogs

TRAMADOL: WHAT DO WE REALLY KNOW?

Sandra Z Perkowski, VMD, PhD, DACVA
University of Pennsylvania School of Veterinary Medicine, Philadelphia, PA

Tramadol is a centrally acting analgesic with low affinity for the mu opioid receptor and with an analgesic action that may be primarily related to inhibition of norepinephrine and serotonin reuptake

The M1 metabolite is the only one shown to be clinically active but has recently been shown to be a relatively minor metabolite in dogs, with plasma levels being lower than those associated with analgesic effects

Pharmacokinetic studies have raised questions regarding appropriate dose and dosing intervals for tramadol and more studies proving efficacy are needed.

Pharmacokinetics in Dogs

- After oral administration in dogs, tramadol is rapidly and extensively metabolized by cytochrome P450 enzymes (CYP) to several metabolites, **only one of which, Odesmethyltramadol (M1), has been shown to be clinically active. O-desmethyltramadol has a much higher affinity (200X) for the mu opioid receptor than the parent compound although the affinity is still only 10% that of morphine.** It was previously suggested that rapid metabolism to the more potent M1 metabolite was responsible for the majority of tramadol's analgesic effect.
- Giorgi et al (2009) found that tramadol was rapidly absorbed after oral administration of an immediate release capsule (4 mg/kg), but then **rapidly metabolized to two other main metabolites the M5 (N,Odesmethyltramadol) and M2 (N-desmethyltramadol) metabolite, rather than the M1 metabolite.** KuKanich and Papich (2011) similarly found **M1 to be a minor metabolite** after a dose of 10mg/kg tramadol in Greyhounds. The **half-lives of both tramadol and all three metabolites were relatively short** (tramadol: 1.1hr vs M1: 1.4 hr).

Tramadol Dosage

Simulated dosing of tramadol suggested that 5 mg/kg q 6 hours or 2.5 mg/kg q 4 hours was required for adequate analgesic levels. This is in contrast to the 2 – 4 mg/kg bid/tid generally recommended.

In human patients, oral tramadol has been shown to be effective in some patients with moderate cancer pain, although efficacy is dependent upon the source of pain, with 83% efficacy in patients with bone pain, but only 33% efficacy in patients with neuropathic pain.

Another study comparing the efficacy of celecoxib vs. tramadol in treatment of patients with chronic low-back pain found celecoxib to be more effective than tramadol, with fewer adverse events.

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Pharmacokinetics of intravenous tramadol in dogs

Chantal J. McMillan, Alex Livingston, Chris R. Clark, Patricia M. Dowling, Susan M. Taylor, Tanya Duke, and Rolf Terlinden

Small Animal Clinical Sciences (McMillan, Duke, Taylor), Veterinary Biomedical Sciences (Livingston, Dowling), and Large Animal Clinical Sciences (Clark), Western College of Veterinary Medicine, 52 Campus Drive, Saskatoon, Saskatchewan S7N 5B4; Department of Pharmacokinetics (PR-ND-PK) Grünenthal GmbH D-52078 Aachen, Germany (Terlinden)

Address all correspondence to Dr. Alex Livingston; telephone: (306) 966-7414; fax: (306) 966-7376; e-mail: ali500@mail.usask.ca

Dr. McMillan's current address is Western Veterinary Specialist Centre, 1802–10th Avenue SW, Calgary, Alberta T2C 0J8.

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Abstract

Go to:

The purpose of this study was to determine the pharmacokinetics of tramadol and the active metabolite mono-O-desmethyltramadol (M1) in 6 healthy male mixed breed dogs following intravenous injection of tramadol at 3 different dose levels. Verification of the metabolism to the active metabolite M1, to which most of the analgesic activity of this agent is attributed to, was a primary goal. Quantification of the parent compound and the M1 metabolite was performed using gas chromatography. Pharmacodynamic evaluations were performed at the time of patient sampling and included assessment of sedation, and evaluation for depression of heart and respiratory rates. This study confirmed that while these dogs were able to produce the active M1 metabolite following intravenous administration of tramadol, the M1 concentrations were lower than previously reported in research beagles. Adverse effects were minimal, with mild dose-related sedation in all dogs and nausea in 1 dog. Analgesia was not documented with the method of assessment used in this study. Tramadol may be useful in canine patients, but additional studies in the canine population are required to more accurately determine the effective clinical use of the drug in dogs and quantification of M1 concentrations in a wider population of patients.

Introduction

Go to:

Control of chronic painful conditions is becoming an increasingly important part of veterinary medicine. Many of the available analgesics are considered effective for a variety of painful conditions in dogs; however, their use may be limited for various reasons. The development of unwanted side effects are a major factor that limits their use, particularly in chronically painful conditions.

Tramadol has only recently gained significant attention as an analgesic in dogs despite its having been used in humans in Germany since 1977 and in North America since the mid 1980's (1). Tramadol has been used as an analgesic in a variety of human conditions (2,3) and has been demonstrated to be as effective as morphine for moderate pain, but less effective for severe acute pain (4). One advantage of tramadol for chronic pain treatment over many other opioids is the absence of strict regulatory measures with regards to its use (4). In addition, tramadol in humans appears to have less potential for abuse, gastrointestinal side effects (5,6) and respiratory depression (7) than conventional opioids.

Tramadol

- Action appears to be predominantly on neurotransmitters (serotonin and norepinephrine)
  - Action similar to fluoxetine
  - Serotonin syndrome is possible (do not use with other SSRIs)
- Blood levels drop dramatically after 14 days of administration
- We are all likely using this drug incorrectly in dogs

Tramadol

- The major reason for the use of tramadol was safety and it was not a controlled substance.
- Use for more than 14 days is likely contra-indicated
- Does not provide analgesia like opioids do
- Does seem somewhat effective. Fluoxetine or Trazadone may be just as effective and are not controlled.

NSAIDs

- NSAIDS have been shown to be as effective as opioids in numerous controlled clinical trials in humans and our pets
- Particularly more effective in dogs than Tramadol
  - Not surprising given Tramadol's lack of mu agonist activity in the dog

Comparison of morphine and carprofen administered alone or in combination for analgesia in dogs undergoing ovariohysterectomy

T B Dzikiti[a*], K E Joubert[a,b], L J Venter[a] and L N Dzikiti[c]

ABSTRACT

In this study the analgesic efficacy of the pure agonistic opioid morphine and the cyclo-oxygenase type-2-selective carprofen were compared since there is no previous specific comparative study for these two common analgesics. Forty-five bitches undergoing elective ovariohysterectomy were randomly assigned to one of three groups; receiving morphine 0.4 mg/kg bodyweight pre-operatively and 0.2 mg/kg every 4–6 hours thereafter (Morphine group), receiving a once-off carprofen 4 mg/kg injection (Carprofen group) or receiving both morphine and carprofen (MorphCarp group). The dogs were premedicated with acepromazine 0.01 mg/kg and induced with either thiopentone 5–10 mg/kg or propofol 4–6 mg/kg. General anaesthesia was maintained with halothane in oxygen. The degree of pain was assessed over a 24-hour period under blinded conditions using a pain scale modified from the University of Melbourne pain scale and the Glasgow composite pain tool. Physiological parameters such as respiratory rate, pulse rate and body temperature were also assessed over the same time period. There was no significant difference in pain-scores and thus analgesia offered by the three analgesia protocols at any assessment point across the three groups, but there were differences within groups across time points. Baseline total pain-scores were lower than scores at all post-operative points within all three groups. Both morphine and carprofen provided good analgesia without any obvious adverse effects. This study indicates that at the dosages indicated above, carprofen administered on its own produces analgesia equal to that produced by morphine and that the two drugs administered together do not produce better analgesia than either drug administered on its own.

Key words: analgesia, balanced analgesia, carprofen, morphine, NSAIDs, opioids, pain.

Dzikiti T B, Joubert K E, Venter L J, Dzikiti L N **Comparison of morphine and carprofen administered alone or in combination for analgesia in dogs undergoing ovariohysterectomy**. *Journal of the South African Veterinary Association* (2006) 77(3): 120–126 (En.). Department of Companion Animal Clinical Studies, Faculty of Veterinary Science, University of Pretoria, Private Bag X04, Onderstepoort, 0110 South Africa

INTRODUCTION

All animals undergoing surgical procedures require pain relief after surgery to overcome the deleterious physiological effects of postoperative pain and to address humane and ethical concerns[18,24]. Non-steroidal anti-inflammatory drugs (NSAIDs), opioid analgesic agents and local anaesthetic agents are the main drugs used to control postoperative pain in animals[6,15,27]. Opioid analgesics have traditionally been the most widely used analgesics in veterinary practice[31].

The classification of opioid analgesics as controlled drugs, concerns regarding their adverse effects and lack of familiarity with opioids available make veterinarians reluctant to use them for pre-emptive analgesia[6,23]. Moreover, opioids are known to cause cardiopulmonary depression and increase depth of sedation and thus prolong recovery, which can, depending on practice circumstances, be interpreted as undesirable effects of opioid use[30,27]. These negative factors associated with opioid use have resulted in the prominence of NSAIDs in providing perioperative analgesia[31]. Despite the desirable analgesic effects of NSAIDs, their use is associated with inhibition of prostaglandin production and disruption of the processes they participate in, resulting principally in various degrees of renal function impairment and gastrointestinal irritation and ulceration[13,24]. Other adverse effects of NSAIDs include coagulopathy, liver damage and worsening of cardiac failure[19]. The NSAID carprofen (6-chloro-alpha-methyl-carbazole-2-acetic acid) is a particular exception in that it produces little or no side-effects, while at the same time providing good efficacy as an analgesic and anti-inflammatory agent[11]. The exact mode of action of carprofen is not understood. There is, however, evidence from *ex vivo* canine studies that it is cyclo-oxygenase (COX) type 2 selective while some authors suggest that it has limited COX activity[1,31]. With a half maximal inhibitory concentration (IC_{50}) ratio, COX-2/COX-1, of 0.04–0.4, carprofen produces preferential inhibition of COX-2 when compared with most other NSAIDs[3,22]. The products of COX-2 are thought to be responsible for the inflammatory process, while cyclo-oxygenase COX-1, which is produced continuously in small quantities is responsible for production of the homeostatic prostaglandin and thromboxane mediators[28,31]. While the hypothesis developed in 1991 that COX-1 inhibition is associated with side-effects while COX-2 inhibition is associated with therapeutic effects still holds true, it has been modified as a result of recent developments such as the discovery of a third COX isoform, COX-3, and evidence of a role for central nervous system actions of NSAIDs as analgesics and anti-inflammatory agents in addition to their peripheral actions[22]. The injectable form of carprofen has undergone extensive use clinically pre-operatively with good effect and few reported side-effects in cats and dogs[3,19].

Despite the fact that opioids and NSAIDs produce their effects by different mechanisms, it is still reasonable to compare the two since they are both used for relief of pain. It is also of interest to determine how combinations of the two would perform since this approach is thought to provide optimal analgesia rather than use of a single analgesic agent[30]. One clinical trial done in 1994 indicated that carprofen at 4 mg/kg preoperatively provided slightly better pain relief than pethidine at 2 mg/kg preoperatively and 3 mg/kg postoperatively[30]. Pethidine is an opioid, which is 10 times less potent than morphine[9]. A more recent study showed that dogs treated with a combination of 4 mg/kg carprofen and 5 mg/kg pethidine

[a]Department of Companion Animal Clinical Studies, Faculty of Veterinary Science, University of Pretoria, Private Bag X04, Onderstepoort, 0110 South Africa.
[b]Fourways Veterinary Hospital, PO Box 68190, Bryanston, 2021 South Africa.
[c]Computational Biology Unit, Department of Biochemistry, Faculty of Natural and Agricultural Sciences, Lynwood Road, Hillcrest, Pretoria, 0002 South Africa.
*Author for correspondence.
E-mail: brighton.dzikiti@up.ac.za
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Abstract

Full text links

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Comparison of carprofen and tramadol for postoperative analgesia in dogs undergoing enucleation.

Delgado C[1], Bentley E, Hetzel S, Smith LJ.

Author information

Abstract

OBJECTIVE: To compare analgesia provided by carprofen and tramadol in dogs after enucleation.

DESIGN: Randomized, masked clinical trial.

ANIMALS: 43 dogs.

PROCEDURES: Client-owned dogs admitted for routine enucleation were randomly assigned to receive either carprofen or tramadol orally 2 hours prior to surgery and 12 hours after the first dose. Dogs were scored for signs of pain at baseline (ie, before carprofen or tramadol administration) and at 0.25, 0.5, 1, 2, 4, 6, 8, 24, and 30 hours after extubation. Dogs received identical premedication and inhalation anesthesia regimens, including premedication with hydromorphone. If the total pain score was ≥ 9 (maximum possible score of 20), there was a score ≥ 3 in any of 5 behavioral categories (highest score possible per category was 3 or 4), or the visual analog scale (VAS) score was ≥ 35 (maximum possible score of 100) combined with a palpation score > 0, rescue analgesia (hydromorphone) was administered and treatment failure was recorded.

RESULTS: No differences were found in age, sex, or baseline pain scores between groups. Significantly more dogs receiving tramadol required rescue analgesia (6/21), compared with dogs receiving carprofen (1/22). Pain and VAS scores decreased linearly over time. No significant differences were found in pain or VAS scores between groups at any time point (dogs were excluded from analysis after rescue).

CONCLUSIONS AND CLINICAL RELEVANCE: Results of this study suggested that carprofen, with opioid premedication, may provide more effective postoperative analgesia than tramadol in dogs undergoing enucleation.

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NIHMSID: NIHMS670299

Carprofen provides better post-operative analgesia than tramadol in dogs after enucleation: A randomized, masked clinical trial

Cherlene Delgado, DVM, Ellison Bentley, DVM, DAVCO, Scott Hetzel, MS, and Lesley J Smith, DVM, DACVAA

Department of Surgical Sciences, School of Veterinary Medicine (Delgado, Bentley, Smith) and Department of Biostatistics and Medical Informatics University of Wisconsin-Madison, Madison WI 53706. Dr. Delgado's current address Bluepearl Veterinary Partners, 820 W Frontage RD, Northfield, IL 60093
Address correspondence to: Dr. Bentley at ; Email: bentleye@svm.vetmed.wisc.edu

Abstract

Go to:

Objective

To compare analgesia provided by carprofen or tramadol in dogs after enucleation.

Design

Randomized, masked trial

Animals

Forty-three dogs

Procedures

Client-owned dogs admitted for routine enucleation were randomly assigned to receive either carprofen or tramadol orally 2 hours prior to surgery and 12 hours after the first dose. Dogs were scored for pain at baseline, and postoperatively at 0.25, 0.5, 1, 2, 4, 6, 8, 24, and 30 hours after extubation. Dogs received identical premedication and inhalation anesthesia regimens, including premedication with hydromorphone. If the total pain score was ≥9, if there was a score ≥ 3 in any one category, or if the visual analog scale score (VAS) was ≥35 combined with a palpation score of >0, rescue analgesia (hydromorphone) was administered and treatment failure was recorded. Characteristics between groups were compared with a Student's t-test and Fisher's exact test. The incidence of rescue was compared between groups using a log rank test. Pain scores and VAS scores between groups were compared using repeated measures ANOVA.

Results

There was no difference in age (p=0.493), gender (p=0.366) or baseline pain scores (p=0.288) between groups. Significantly more dogs receiving tramadol required rescue analgesia (6/21) compared to dogs receiving carprofen (1/22; p=0.035). Pain and VAS scores decreased linearly over time (p=0.038, p<0.001, respectively). There were no significant differences in pain (p=0.915) or VAS scores (p=0.372) between groups at any time point (dogs were

J Am Vet Med Assoc. 2013 Jul 15;243(2):225-31. doi: 10.2460/javma.243.2.225.

Comparison of the analgesic efficacy of perioperative firocoxib and tramadol administration in dogs undergoing tibial plateau leveling osteotomy.

Davila D[1], Keeshen TP, Evans RB, Conzemius MG.

Author information

Abstract

OBJECTIVE: To evaluate the effects of perioperative oral administration of tramadol, firocoxib, and a tramadol-firocoxib combination on signs of pain and limb function after tibial plateau leveling osteotomy in dogs.

DESIGN: Randomized, blinded, prospective clinical trial.

ANIMALS: 30 adult client-owned dogs with unilateral cranial cruciate ligament disease.

PROCEDURES: Dogs were allocated into 3 treatment groups (tramadol, firocoxib, and a tramadol-firocoxib combination). Signs of pain (short-form Glasgow composite measure pain scale), serum cortisol concentrations, and limb function (pressure platform gait analysis) were recorded at several time points before surgery and through 3 days after surgery. Outcome measures were compared among groups.

RESULTS: A significantly greater number of dogs in the tramadol group (8/10 dogs) had a pain score > 6 after surgery, compared with the other groups. No significant differences were detected in the pain scores between the firocoxib and the tramadol-firocoxib combination groups. There were no significant differences in serum cortisol concentrations among the 3 groups. Limb function was significantly decreased for dogs in the tramadol group on days 1 and 2 after surgery and in the firocoxib group on day 1 after surgery. Although limb function decreased for dogs in the tramadol-firocoxib combination group, the change was not significant for any day after surgery.

CONCLUSIONS AND CLINICAL RELEVANCE: Dogs that received firocoxib orally, alone or in combination with tramadol, had lower pain scores, lower rescue opiate administration, and greater limb function than dogs that received only tramadol. When used alone, oral administration of tramadol may not provide sufficient analgesic efficacy to treat dogs with pain after orthopedic surgical procedures.

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NSAIDs: Dogs

- A variety of injectable and oral NSAIDs available
- Cox2 inhibitors can be mixed and matched
  - Carprofen
  - Meloxicam
  - Deracoxib
  - Firocoxib
  - Robenicoxib
  - Grapiprant: EP4 inhibitor

NSAIDs: dogs

- Carprofen is the least selective Cox 2 inhibitor
- Can cause reversible platelet inhibition
- Prefer to avoid use 12-24 hours pre-operatively

Other NSAIDs

- No justification for use of older NSAIDs
  - Off label use
  - More side effects
  - Aspirin should not be used with surgery

NSAID: cats

- Both Meloxicam and Robenicoxib can be used safely in cats
  - Meloxicam licensed for use in cats in Europe
  - Off label use in US (black box warning!!)
  - Robenicoxib approved for long term use in cats in other countries
    - Even aspirin can be used safely in cats, given at the correct dose (low dose: 81mgs q 72 hours), but you didn't hear that from me

Abstract

Full text links

View Full-Text Article at SAGE Publications

J Feline Med Surg. 2008 Jul;10(3):235-41. doi: 10.1016/j.jfms.2007.10.007. Epub 2008 Apr 28.

Long-term safety, efficacy and palatability of oral meloxicam at 0.01-0.03 mg/kg for treatment of osteoarthritic pain in cats.

Gunew MN[1], Menrath VH, Marshall RD.

Author information

Abstract

Osteoarthritis is a chronic, painful condition that is now recognised as affecting a large proportion of cats. Non-steroidal anti-inflammatory drugs (NSAIDs) have proven efficacy in dogs and humans but there are limited published data on the use of NSAIDs in the long-term management of this condition in cats. This prospective study aimed to assess the long-term safety and palatability of oral meloxicam and its efficacy in treating osteoarthritic pain in cats when given at a dose of 0.01-0.03 mg/kg once daily. Forty cats diagnosed with osteoarthritis completed the trial with a mean treatment duration of 5.8 months. Gastrointestinal upset in 2/46 (4%) cats was the only adverse effect noted. No deleterious effect on renal function was detected in cats studied. Owners subjectively assessed treatment efficacy as good or excellent in 34/40 (85%) of cases. The results of this study showed oral meloxicam to be safe and palatable long-term treatment for osteoarthritis in cats when given with food at a dose of 0.01-0.03 mg/kg.

PMID: 18440263 [PubMed - indexed for MEDLINE]

Publication Types, MeSH Terms, Substances

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Am J Vet Res. 2013 Apr;74(4):648-51. doi: 10.2460/ajvr.74.4.648.

Evaluation of glomerular filtration rate in cats with reduced renal mass and administered meloxicam and acetylsalicylic acid.

Surdyk KK[1], Brown CA, Brown SA.

Author information

Abstract

OBJECTIVE: To determine whether administration of meloxicam or acetylsalicylic acid alters glomerular filtration rate (GFR) in cats with renal azotemia.

ANIMALS: 6 young adult cats.

PROCEDURES: 3 sexually intact male cats and 3 sexually intact female cats had surgically reduced renal mass and azotemia comparable to International Renal Interest Society chronic kidney disease stages 2 and 3. Renal function was evaluated by measurement of serum creatinine concentration, urinary clearance of exogenously administered creatinine, and the urine protein-to-creatinine concentration ratio (UP:C). Measurements taken in cats receiving placebo at the beginning and end of the study were compared with results obtained at the end of 7 days of treatment with either meloxicam (0.2 mg/kg, SC, on day 1; 0.1 mg/kg, SC, on days 2 to 7) or acetylsalicylic acid (20 mg/kg, PO, on days 1, 4, and 7).

RESULTS: No significant treatment effects on urinary clearance of exogenously administered creatinine, serum creatinine concentration, or UP:C were detected. Mean ± SEM serum creatinine concentration and urinary clearance of exogenously administered creatinine measurements following 7 days of treatment with meloxicam (serum creatinine concentration, 2.67 ± 0.17 mg/dL; urinary clearance of exogenously administered creatinine, 1.34 ± 0.08 mL/min/kg) and acetylsalicylic acid (serum creatinine concentration, 2.62 ± 0.12 mg/dL; urinary clearance of exogenously administered creatinine, 1.35 ± 0.07 mL/min/kg) were not significantly different from the mean baseline values for these variables (serum creatinine concentration, 2.77 ± 0.14 mg/dL; urinary clearance of exogenously administered creatinine, 1.36 ± 0.07 mL/min/kg).

CONCLUSIONS AND CLINICAL RELEVANCE: Neither meloxicam nor acetylsalicylic acid had a measurable effect on urinary clearance of exogenously administered creatinine, serum creatinine concentration, or UP:C. These results are consistent with the hypothesis that GFR of euvolemic cats with normal or reduced renal function is not dependent on cyclooxygenase function.

PMID: 23531076 [PubMed - indexed for MEDLINE]

J Feline Med Surg. 2011 Oct;13(10):752-61. doi: 10.1016/j.jfms.2011.06.008. Epub 2011 Sep 9.

Retrospective case-control study of the effects of long-term dosing with meloxicam on renal function in aged cats with degenerative joint disease.

Gowan RA[1], Lingard AE, Johnston L, Stansen W, Brown SA, Malik R.

Author information

Abstract

Medical records (2005-2009) of a feline-only practice were searched for cats with degenerative joint disease (DJD) treated using meloxicam. DJD was diagnosed by the presence of at least two of the following: (i) altered mobility (observed by the owner), (ii) abnormal physical findings, (iii) characteristic radiographic changes. The primary study cohort consisted of cats older than 7 years that had received meloxicam for variable intervals in excess of 6 months, and for which complete records were available. These cats were subdivided according to whether detectable chronic kidney disease (CKD) was present ('renal group'), or not ('non-renal group'), and, for the 'renal group', according to the cat's IRIS category. Serum biochemistry, urinalysis (including urine specific gravity [USG]), body mass and condition score were monitored regularly. Progression of CKD in the 'renal group' and 'non-renal group' of cats was compared to two groups of age- and IRIS-matched control cats not receiving meloxicam (from the same clinic, over the same time period). The study was thus a case-control design, with two study groups. Thirty-eight cats with DJD receiving long-term meloxicam therapy met the inclusion criteria. Of these, 22 cats had stable CKD at the start of treatment (stage 1, eight cats; stage 2, 13 cats; stage 3, one cat). No cats initially had an elevated urinary protein to creatinine ratio. The remaining 16 cats initially had normal renal analytes and adequately concentrated urine. The median age of the 'renal' and 'non-renal' meloxicam groups was 15.5 and 13.4 years, respectively. The median treatment duration was 467 days in the 'renal group' and 327 days in the 'non-renal group'. After titration (to the lowest effective dose), the median maintenance dose was 0.02 mg/kg/day in both groups (range 0.015-0.033 mg/kg/day). There was no difference in sequential serum creatinine concentration or USG measurements between the 'non-renal group' treated with meloxicam compared to control cats not treated with meloxicam. There was less progression of renal disease in the 'renal group' treated with meloxicam compared to the age- and IRIS-matched cats with CKD not given meloxicam. These results suggest that a long-term maintenance dose of 0.02 mg/kg of meloxicam can be safely administered to cats older than 7 years even if they have CKD, provided their overall clinical status is stable. Long-term meloxicam therapy may slow the progression of renal disease in some cats suffering from both CKD and DJD. Prospective studies are required to confirm these findings.

NSAIDs: Cats

- Feline renal function does not depend on the cyclooxygenase pathways
- Dosage of meloxicam in cats is significantly lower than in dogs (0.03-0.05 mgs/kg q daily)
  - Previous reports leading to black box label were based on dramatically higher dosages
- Use Robenicoxib if you wish to avoid off-label use of Meloxicam. However, use beyond 3 days is off-label in US (but not Europe/Australia)

NSAIDs

- DO NOT GIVE NSAIDS TO ANY PATIENT WHO IS ON OR WHO HAS RECEIVED STEROIDS WITHIN 72 HOURS

Other Modalities

- Gabapentin
  - Indicated for neurogenic pain (not nociceptive pain)
  - Despite the frequent recommendation for using gabapentin to manage chronic pain in dogs, there is little data available evaluating its efficacy. A double blinded study did not find a short-term benefit of gabapentin on postsurgical pain.
- Trazadone
  - Large safety margin
  - SSRI
  - Probably very similar to Tramadol in dogs
  - Seems as effective as Tramadol IMHO
  - Not a controlled drug

Other Modalities

- Neuraxial Anesthesia
  - Epidural and intrathecal pain control
  - Opioids or lidocaine
  - Preservative free
  - Can be quite effective, learning curve required
  - Most useful for pelvic limb procedures
  - Possibility of respiratory depression, bradycardia, and sympathetic blockade

Other Modalities

- Local blocks: local anesthesia given before or during surgery
  - Particularly effective for thoracotomy and amputation
  - Can be given IA
  - Topical, local infiltration, nerve blocks, distal limb blocks, brachial plexus blocks, intercostal nerve block, MUMR block
  - Bupivicaine lasts longer than lidocaine
  - Nocita (bupivacaine liposome)

Nocita

- Bupivicaine liposome suspension
- 72 hours of post-operative analgesia
- Extended release formula
- Limited lifespan once vial is opened
- Infiltration of each tissue layer at closure
- Expense
- Only approved use is TPLO

Questions??

Induction Adjuvants

- • Dexmedetomidine (0.5-1 gg/kg IV) **or**
- • Medetomidine (1-2 gg/kg IV) ***plus***
- • Ketamine (0.5-1 mg/kg IV) ***plus***
- • Fentanyl (2-10 mg/kg IV PRN: *for short term pain relief*)

CRI

- Hydromorphone (0.025-0.1 mg/kg/hr IV) ***or*** **Fentanyl** (1-10 mcg/kg/hr loading dose), then10-30 mcg/kg/hr intraoperatively and 2-20 mcg/kg/hr IV postoperatively
- Dexmedetomidine (2.5-5 mcg/kg IV loading dose),then 0.5-1 mcg/kg/hr
- Ketamine (0.5 mg/kg IV loading dose), then 10 mcg/kg/min IV CRI intraoperatively and 2 mcg/kg/min IV CRI postoperatively
- FLK
  - Fentanyl (1-5 mcg/kg/hr IV) ***plus***
  - Lidocaine (25-50 mcg/kg/min IV) ***plus***
  - Ketamine (2-5 mcg/kg/min IV)
- MLK (not recommended for cats)
  - Morphine (3.3 mcg/kg/min IV) ***plus***
  - Lidocaine (50 mcg/kg/min IV) ***plus***
  - Ketamine (10 µg/kg/min IV)

- HYDROMORPHONE- Dogs: 0.1-0.4mg/kg IM/SQ/IV Cats: 0.05-0.2mg/kg IM/SQ/IV **vomiting is more common after IM administration. Onset 10-20 minutes, duration 4-8 hours.
- OXYMORPHONE- Dogs: 0.05-.2mg/kg IM/SQ/IV Cats: 0.025-0.1 mg/kg IM/SQ/IV. Rapid onset, duration 4-6 hours.
- MORPHINE- Dogs: 0.5-1mg/kg IM/SQ/IV Cats: 0.25-.05mg/kg IM/SQ/IV. Rapid onset, duration 4- 6 hours. Potential to cause transient hypotension, often causes vomiting with IM or SQ use, and may cause histamine release with IV use.
- FENTANYL- Loading dose of 2-5 ug/kg followed by 2-45 ug/kg/hr IV CRI. Note- if animal is premedicated with another pure mu agonist, it may not be necessary to give a loading dose of the fentanyl.
- METHADONE- Dogs: 0.5 to 1.0 mg/kg IM/SQ/IV Cats: 0.25 to 0.5 mg/kg IM/SQ/ slow IV. Rapid onset, duration 4-6 hours. Least likely to cause vomiting.
- BUPRENORPHINE- Dogs: 0.005-0.03 mg/kg IM/SQ/IV Cats: 0.005-0.01mg/kg IM/SQ/IV, 0.005- 0.03 buccal. Onset 30-60 minutes, duration 4-12 hours depending on the dose.
- BUTORPHANOL- 0.1-.04mg/kg IM/SQ/IV. Rapid onset, duration 1-3 hours. Not recommended for somatic (orthopedic/joint/muscle) pain.

- CODEINE: 0.5-2mg/kg PO BID-QID.
- TYLENOL/HYDROCODONE: 0.22-0.5 mgs/kg Hydrocodone. Do not exceed 15/mg/kg Acetaminophen
  - 20 kg dogs or larger for tablets
  - Liquid for smaller patients

Hydrocodone/Acetaminophen Oral Tablets: 5 mg/300 mg, 5 mg/325 mg, 7.5 mg/300 mg, 7.5 mg/325 mg, 10 mg/300 mg, & 10 mg/325 mg.

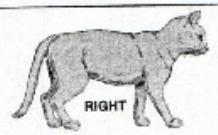
An oral solution containing hydrocodone 2.5 mg/5 mL in combination with acetaminophen 167 mg/5 mL (0.5 mg/mL hydrocodone and 33.3 mg/mL of acetaminophen) is also readily available. Commonly used trade names for these products include: *Vicodin*®, *Norco*®, and *Lortabs*®. They are all Rx; C-II in the USA.

Date _____

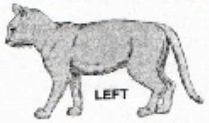
Time _____

Rescore when awake ☐ **Animal is sleeping, but can be aroused - Not evaluated for pain** ☐ **Animal can't be aroused, check vital signs, assess therapy**

Pain Score	Example	Psychological & Behavioral	Response to Palpation	Body Tension
0		☐ **Content and quiet** when unattended ☐ **Comfortable** when resting ☐ Interested in or **curious** about surroundings	☐ **Not bothered** by palpation of wound or surgery site, or to palpation elsewhere	Minimal
1		☐ **Signs are often subtle and not easily detected in the hospital setting**; more likely to be detected by the owner(s) at home ☐ Earliest signs at home may be **withdrawal from surroundings or change in normal routine** ☐ In the hospital, may be content or slightly unsettled ☐ **Less interested** in surroundings but will look around to see what is going on	☐ May or may not react to palpation of wound or surgery site	Mild
2		☐ Decreased responsiveness, **seeks solitude** ☐ **Quiet**, loss of brightness in eyes ☐ **Lays curled up or sits tucked up** (all four feet under body, shoulders hunched, head held slightly lower than shoulders, tail curled tightly around body) with eyes partially or mostly closed ☐ **Hair coat appears rough** or fluffed up ☐ May intensively groom an area that is painful or irritating ☐ Decreased appetite, **not interested in food**	☐ **Responds aggressively or tries to escape** if painful area is palpated or approached ☐ Tolerates attention, may even perk up when petted as long as painful area is avoided	Mild to Moderate **Reassess analgesic plan**
3		☐ Constantly **yowling, growling, or hissing** when unattended ☐ May bite or chew at wound, but **unlikely to move** if left alone	☐ **Growls or hisses at non-painful palpation** (may be experiencing allodynia, wind-up, or fearful that pain could be made worse) ☐ **Reacts aggressively** to palpation, **adamantly pulls away** to avoid any contact	Moderate **Reassess analgesic plan**
4		☐ Prostrate ☐ Potentially **unresponsive** to or unaware of surroundings, difficult to distract from pain ☐ Receptive to care (even mean or wild cats will be more tolerant of contact)	☐ **May not respond** to palpation ☐ **May be rigid to avoid painful movement**	Moderate to Severe **Reassess analgesic plan**



○ Tender to palpation
✕ Warm
■ Tense



Comments _____

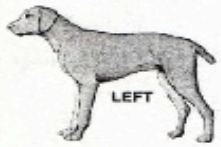
Date _____

Time _____

Rescore when awake ☐ **Animal is sleeping, but can be aroused - Not evaluated for pain**
☐ **Animal can't be aroused, check vital signs, assess therapy**

Pain Score	Example	Psychological & Behavioral	Response to Palpation	Body Tension
0		☐ **Comfortable** when resting ☐ **Happy, content** ☐ Not bothering wound or surgery site ☐ Interested in or curious about surroundings	☐ **Nontender** to palpation of wound or surgery site, or to palpation elsewhere	Minimal
1		☐ **Content to slightly unsettled** or restless ☐ **Distracted easily** by surroundings	☐ **Reacts to palpation** of wound, surgery site, or other body part by **looking around, flinching,** or **whimpering**	Mild
2		☐ Looks **uncomfortable** when resting ☐ May **whimper** or cry and may **lick or rub wound** or surgery site when unattended ☐ Droopy ears, **worried facial expression** (arched eye brows, darting eyes) ☐ **Reluctant to respond** when beckoned ☐ **Not eager to interact** with people or surroundings but will look around to see what is going on	☐ Flinches, whimpers, cries, or guards/pulls away	Mild to Moderate **Reassess analgesic plan**
3		☐ **Unsettled, crying, groaning, biting or chewing** wound when unattended ☐ **Guards or protects** wound or surgery site by altering weight distribution (i.e., limping, shifting body position) ☐ **May be unwilling to move** all or part of body	☐ May be **subtle** (shifting eyes or increased respiratory rate) if dog is too painful to move or is stoic ☐ May be **dramatic**, such as a sharp cry, growl, bite or bite threat, and/or pulling away	Moderate **Reassess analgesic plan**
4		☐ **Constantly groaning or screaming** when unattended ☐ May bite or chew at wound, but unlikely to move ☐ **Potentially unresponsive** to surroundings ☐ **Difficult to distract** from pain	☐ **Cries at non-painful palpation** (may be experiencing allodynia, wind-up, or fearful that pain could be made worse) ☐ May react aggressively to palpation	Moderate to Severe **May be rigid to avoid painful movement** **Reassess analgesic plan**

○ Tender to palpation
✕ Warm
■ Tense



Comments _____

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